REMARKS

A. Status of the Claims

Claims 12-35 were pending at the time of the Action, with claims 21-34 being withdrawn from consideration by the Examiner as being drawn to a non-elected invention(s). Claim 12 has been amended to incorporate the subject matter of claims 13-15, which have now been canceled. Claims 17 and 18 have been amended to maintain proper antecedent basis in view of the amendment to claim 12. Claim 21 has been amended to incorporate the subject matter of claims 24-26, which have now been canceled. Claims 27-29 have been amended to maintain proper antecedent basis in view of the amendment to claim 21. Claim 34 has been amended to recite "tumor or cancer cells." Support for this amendment may be found in the specification at, for example, paragraphs [0023], [0024], [0027], and [0036]-[0038] (as numbered in Publication No. 2006/0127349). Claim 35 has been amended to replace "poly-N-vinylamide" with "polyvinylpyrrolidone." Support for this amendment may be found in the specification at, for example, paragraph [0015]. Claims 12 and 35 have also been amended to recite that the water-soluble complex is "in an aqueous solution." Support for this amendment may be found in the specification at, for example, paragraphs [0011], [0014], and [0020]. Claims 19-20 and 30-33 have been canceled without prejudice or disclaimer. Thus, claims 12, 16-18, 21-29, and 34-35 are now pending, with claims 12, 16-18, and 35 currently under examination.

B. The Claims Are Novel Over Cody, Bombardelli, and Castillo

The Action rejects claims 12-14, 19 and 20 under 35 U.S.C. § 102(b) as being anticipated by Cody (U.S. Patent No. 6,063,401) and claims 12-14 and 19 under 35 U.S.C. § 102(e) as being anticipated by either Bombardelli (U.S. 2001/0000326) or Castillo (U.S. 2002/0150637). Claim 15 was indicated to be novel over the Cody, Bombardelli, and Castillo references. To advance

the prosecution of this application, Applicant has incorporated the subject matter of claim 15 into claim 12. Applicant, therefore, requests the withdrawal of these rejections.

C. The Claims Are Patentable Over Cody and JP 409262279

Claims 12-20 and 35 are rejected under 35 U.S.C. § 103(a) as being obvious over Cody in view of JP 409262279 ("the '279 publication"). The Action asserts that Cody teaches a soft gelatin capsule containing *Hypericum perforatum* and polyvinylpyrrolidone. The Action further asserts that while Cody does not teach that the polyvinylpyrrolidone is 10,000-40,000 g/mol, the '279 publication makes up for this deficiency. Applicant traverses this rejection.

Hypericin is naturally a lipidic and water-insoluble compound that makes its application in the human body difficult (Specification, para. [0003]). The present inventors, however, have demonstrated that hypericin can be rendered water-soluble when complexed with a poly-N-vinylamide such as polyvinylpyrrolidone (PVP). (Specification, para. [0011]). As a result of complexing hypericin with PVP, a water-soluble form of hypericin is available in an aqueous solution for the first time in physiologically relevant amounts (Specification, para. [0011]).

The complexing of hypericin and PVP in an aqueous solution was also shown to have special selectivity that results in the substance concentrating in tumor cells (Specification, para. [0027]). For example, when a water-soluble complex of a hypericin-PVP complex in an aqueous solution was instilled into the bladders of four patients with well differentiated bladder tumors, a clear fluorescence of tumors in the bladder was observed (Specification, para. [0036]). The water solubility of the hypericin-PVP complex was important in this regard because uncomplexed hypericin in an aqueous environment forms insoluble aggregates that do not fluoresce after stimulation (*see* Specification, FIG. 1 and corresponding text and para. [0034]). Additionally, low molecular weights (i.e., 10,000 – 90,000 g/mol) of PVP are employed to facilitate diffusion through cell membranes (Specification, para. [0015]).

Cody does not disclose a composition comprising a water-soluble complex of hypericin and PVP in an aqueous solution. While polyvinylpyrrolidone is mentioned in Cody as a suitable solvent for the liquid cores of gel capsules in to which *Hypericum perforatum* may be added, Cody does not teach a complex of a synthetic or isolated hypericin and polyvinylpyrrolidone in an aqueous solution. Cody appears to disclose only organic solvents. *See* col. 5, line 59 through col. 6, line 6. Moreover, these organic solvents appear to be merely auxiliary agents for forming gel capsules.

Cody also does not specifically disclose the use of low molecular weights (i.e., 10,000 – 90,000 g/mol) of PVP. The Action notes that the '279 publication indicates that PVP having molecular weights of 20,000-150,000 were know. However, even though the '279 publication discloses a partially overlapping range of PVP molecular weights, there is no apparent reason as to why a person of ordinary skill in the art would have combined the elements of Cody and the '279 publication in the fashion currently claimed. Cody was concerned with orally ingestible capsules or pills, whereas the '279 publication was concerned with making adhesives. Thus, neither was concerned with the need for a low molecular weight PVP (i.e., 10,000-90,000 g/mol), such as would be beneficial for facilitating diffusion of a hypericin-PVP complex through cell membranes.

As discussed above, the presently claimed composition surprisingly rendered hypericin water-soluble and exhibited selectivity to tumor cells. These results would not have predictable to one of ordinary skill in the art based on the teachings of Cody and the '279 publication. When combined elements work together in an unexpected and fruitful manner, this is evidence that the combination was not obvious. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007).

For at least the reasons above, the current claims are patentable over Cody and the '279 publication. Applicants, therefore, request the withdrawal of the rejection.

D. The Claims Are Patentable Over Bombardelli *et al.* or Castillo *et al.* in View of Cody and JP 409262279

The Action rejects claims 12-20 and 35 under 35 U.S.C. § 103(a) as obvious over Bombardelli *et al.* or Castillo in view of Cody and the '279 publication. The Action asserts that Bombardelli *et al.* and Castillo each teach a tablet containing *Hypericum perforatum* and polyvinylpyrrolidone. The Action further states that while Bombardelli *et al.* and Castillo do not teach that the polyvinylpyrrolidone has the claimed molecular weight, the other amounts in the claims, or a composition in gel form, Cody and the '279 publication make up for these deficiencies. Applicant traverses this rejection.

As with the Cody reference (see preceding section), the Bombardelli and Castillo references also do not teach or suggest a composition comprising a water-soluble complex of hypericin and a polyvinylpyrrolidone having a molecular weight from 10,000 to 90,000 g/mol in an aqueous solution. In fact, Bombardelli teaches that the aqueous phase is removed from the extract of *Hypericum perforatum* and the extract is dried under a vacuum (Example 2, para. [0039]). Moreover, the only context in which it appears that PVP is mentioned in the presence of a *Hypericum perforatum* extract is in paragraph [0041], wherein a tablet comprises 5 mg of polyvinylpyrrolidone and 300 mg of the dried extract. In other words, the PVP compound is only an auxiliary for tablet forming and, therefore, no bonding exists between hypercin and the PVP compound. Thus, there is no teaching or suggestion that the polyvinylpyrrolidone and the hypericin are in a complex; and they clearly are not in a water-soluble complex in an aqueous solution. Water is not mentioned in the tablet of paragraph [0041], and, as noted above, the *Hypericum perforatum* extract prepared according to Bombardelli's Example 2 has been dried.

Castillo states that 120 mg of *Hypericum perforatum* and 8 mg of polyvinylpyrrolidone and other components are mixed as powders and ultimately compressed into tablet form on a tablet machine (Castillo, para. [0116]). Thus, as with Bombardelli, the PVP compound in Castillo is only an auxiliary for tablet forming and, therefore, no bonding exists between hypercin and the PVP compound. Accordingly, Castillo also does not teach a water-soluble complex of hypericin and PVP in an aqueous solution.

The Action cites to the '279 publication as teaching that PVP with molecular weights of 20,000-150,000 were know. However, even though the '279 publication discloses a partially overlapping range of PVP molecular weights, there is no apparent reason as to why a person of ordinary skill in the art would have combined the elements of Bombardelli or Castillo with the '279 publication in the fashion currently claimed. Bombardelli and Castillo disclose PVP as a non-active component of tablets, Cody used PVP in orally ingestible capsules or pills, and the '279 publication was used PVP to make adhesives. Thus, none of these references was concerned with the need for a low molecular weight PVP (i.e., 10,000-90,000 g/mol), such as would be beneficial for facilitating diffusion of a hypericin-PVP complex through cell membranes.

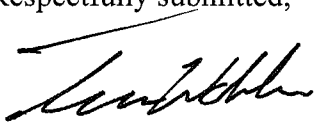
As discussed above, the presently claimed composition surprisingly rendered hypericin water-soluble and exhibited selectivity to tumor cells. These results would not have predictable to one of ordinary skill in the art based on the teachings of Bombardelli, Castillo, Cody, and the '279 publication. When combined elements work together in an unexpected and fruitful manner, this is evidence that the combination was not obvious. *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727, 1740 (2007).

For at least the reasons above, the current claims are patentable over Bombardelli, Castillo, Cody, and the '279 publication. Applicant, therefore, requests the withdrawal of the rejection.

E. Conclusion

In view of the foregoing, Applicants submit that the claims are in condition for allowance and an early indication to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney at (512) 536-5654 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,



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Date: January 29, 2008